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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,459	12/22/1999	MARK D. FIDOCK	PC10315AGPR	7428

7590

08/29/2003

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EXAMINER

SAIDHA, TEKCHAND

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 08/29/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/471,459

Applicant(s)

FIDOCK, MARK D.

Examiner

Tekchand Saidha

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 1899.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1,2,17,29-31 and 36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-2, 17, 29-31 & 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

Final Rejection

1. The Amendment & response filed May 15, 2003 (Paper No. 20) is acknowledged.
2. Group I claims 1-2, 17, 29-31 & 36), species SEQ ID NO : 5 are pending and under consideration in this examination. Claim 16 was withdrawn with other non-elected claims. Prior Office Action Summary mistakenly identifies claim 16 as pending, which has been corrected, and the status of claim 16 is 'withdrawn'. Please make a note of it.

3. ***Election***

Applicants have not responded to arguments presented in the prior Office Action pertaining to distinctiveness of each of the sequences (DNA or protein) and the finality of the restriction requirement, and continue to include SEQ ID Nos. 1 & 3 into the claims. SEQ ID Nos. 1 & 3 are not under consideration.

4. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

5. ***Claim Rejections - 35 U.S.C. § 112 (first paragraph)***

Deposit Requirement

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the [plasmid/microorganism/vector] is required to practice the claimed invention. As such the [plasmid/microorganism/vector] must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be

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satisfied by a deposit of the [plasmid/microorganism/vector]. The specification lacks complete deposit information for the deposit of [plasmid/microorganism/vector]. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, (c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

Claim 17 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

While deposits of NCIMB Numbers 40995, 40996 & 41027 have been made in accordance Budapest Treaty at a recognized depository; however, an affidavit or declaration [under 37 CFR 1.808] stating that : all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, the deposit will be maintained in a public

depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, and the deposit will be replaced if it should ever become inviable.

Applicant's Arguments

Applicant argues that since the deposits were made according to the Budapest Treaty, therefore the necessary declarations cited by the Examiner are already made.

In response, the specification does not contain no such declaration. Therefore, a separate declaration under 37 CFR 1.808 (see the underlined portion) must be made of record before this rejection can be withdrawn.

6. ***Enablement***

Claims 1-2 & 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated PDE of SEQ ID NO: 5 and using cAMP as the substrate, does not reasonably provide enablement for any amino acid sequence of Formula I or a variant, fragment or derivative thereof (claim 1) or isolated PDE_XIV protein that share 75%, 85% or 95% sequence homology to SEQ ID NO : 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. [For convenience, the PDE of the present invention is referred to as PDE_XIV, see specification - page 6].

Claim 1-2 encompass any protein, which by definition of Formula I comprise one or more peptide sequences or amino acids Z1-Z26 (see page 5, substitute specification) or a variant, fragment or derivative thereof; claims 29-31 encompass modifications of SEQ ID NO : 5 by 25%, 15% or 5%. The scope of the claims is not commensurate with the enablement provided

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by the disclosure with regard to the extremely large number of proteins fragments or amino acid or phosphodiesterases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of PDE_XIV.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any protein of the formula I or an isolated PDE_XIV with 75, 85 or 90% identity to the enzyme of SEQ ID Nos: 5 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting PDE_XIV activity; (B) the general tolerance of PDE_XIV to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any PDE_XIV residues with an expectation of

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obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Further, the phosphodiesterases/isozymes from different sources having varying substrate specificities for cAMP or cGMP and the PDE activity in some tissues could be activated by calcium or calmodulin [Beavo et al. (1995), Physiological Reviews 75(4) : 725-748; also see instant specification, page 1-2]. Therefore, random modifications of the SEQ ID NO : 5 or the fragments or derivatives of Formula I, without adequate guidance, may result in a protein with no or entirely diverse PDE activity with different substrate specificity and cofactor requirement.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including PDE_XIV with an enormous number of amino acid modifications of the PDE_XIV of SEQ ID Nos: 5 and retain PDE_XIV activity in the hydrolysis of cAMP as the only substrate for catalysis. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of PDE_XIV having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicant's Arguments -

Applicant argues and disagrees with the Examiner without addressing the rejection in its entirety. The only point the Applicants make is 'All one of ordinary skill in the art need to do is

make a desired modification of the sequences disclosed in the specification and test for PDE activity of the resultant protein using the simple assay provided in the specification on page 78.

Indeed phosphodiesterase assay is provided on page 80 of the instant specification [perhaps a page shift between Applicant's copy and the copy provided to the USPTO] and is sufficient to assay for the PDE activity. But the crucial questions are the numerous modifications that one of ordinary skill in the art has to make to SEQ ID NO : 5 in order to create sequences of various homologies or make variants homologues, fragments or derivatives with no guidance. Further the sequence that comprise Formula I sequences, where in Formula I by definition in the specification comprises one or more peptide sequences or amino acids Z1-Z26, where none of the short peptide sequences have demonstrated PDE activity. Further, many of the key issues of the rejection remain unaddressed.

7. *35 U.S.C. § 112, first paragraph (Written Description)*

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 1-2 recite [or mean as per definition of formula I] 'variant, homologue, fragment or derivative of Formula I'. However, no variant, homologue or derivative of Formula I...is given in the specification.

The specification, however, only provides a single representative species in the generic formula I comprising fragments Z1-Z26. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such

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sequences are conserved in order to establish a relationship among species or modify the sequence(s) of formula I (SEQ ID Nos : 9-22 and the shorter fragments of less than 4 amino acid long, page 5 of the specification) by substitution, deletion or addition (see specification, page 38) or make a polypeptide of an unknown activity. The specification also fails to describe additional representative species of such peptides by any activity other than the identifying structural characteristics recited in Formula I, for which no predictability of activity is apparent. Given this lack of additional representative species, such as the modifications in order to create a variant, homologue, fragment or derivative of Formula I of and still have some activity and/or utility, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Therefore, the written description requirement is not satisfied.

Applicant's Arguments -

Applicant argues that while it is correct that the Applicant has not presented a listing of variants or homologs or homologous SEQ ID NO : 5 sequences (PDE), such is not necessary and those skilled in the art readily understand which variants are likely to retain PDE activity.

It is not clear how without even a single example of sequence modification or the possession of a single disclosed variant or homolog, how a skilled artisan would recognize that Applicant was in possession of the claimed invention.

8.

Claim Rejections - 35 U.S.C. § 112 (second paragraph)

Claims 1-2 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 refer to 'Formula I' - where the formula is represented by **any one** of the amino acids or SEQ ID Nos. (Z1-Z26) as disclosed on page 5 of the substitute specification. While such a formula is meaningless, as nothing is calculated or derived from it, it is also indefinite and unclear with respect to Z2, Z3, Z4, Z8, Z19-Z29, which amino acids/peptide sequences have no reference SEQ ID NO : Clarification and assigning of reference SEQ ID NO : will overcome this rejection.

Since Applicants have elected Group I and species SEQ ID NO : 5 for prosecution, it is unclear from the specification which of the DNA sequences encoding SEQ ID NO : 5 is contained in the 3 deposit numbers (NCIMB) of claim 17.

Clarifying the single deposit and limiting the claim to the specific deposit will overcome this rejection.

Applicant's Arguments -

Applicant argues that the rejection is rendered moot in part by the amendments to claim 1 & 2 and that claims 1 & 2 now require that the claimed amino acid sequences include SEQ ID NO : 1, 3 or 5. However, this is not the case, the claims still recite formula I, which by definition remains obscure and indefinite as explained above.

The reasons for indefiniteness is the recitation of Formula I and not in the inclusion of non-elected invention [SEQ ID NO : 1 or 3 or the DNA connected deposit numbers].

Applicant's argument is well taken. However, Applicants continue to include SEQ ID Nos. 1, 3 or 5, with the clear knowledge that the Applicant has elected species SEQ ID NO : 5 for prosecution. Similarly, the deposit containing the nucleic acid encoding SEQ ID NO : 5 is under consideration only.

9. **Priority:** In evaluating the prior art, Applicants were deemed to be entitled to an effective filing date of **9.17.99**, the filing date of foreign application filed in United Kingdom 9922123.6, with respect to the complete or claimed human sequence of PDE_XIV (450 amino acids).

The human sequence of PDE_XIV (SEQ ID NO : 2) as disclosed in United Kingdom 9828603.2, filed 12.23.98, had only **288 amino acids** as compared to instantly claimed human sequence of PDE_XIV (SEQ ID NO : 5) having 450 amino acids. Therefore, United Kingdom 9828603.2, does not qualify for the earlier priority of 12.23.98, because this priority document was lacking an enabling disclosure with respect to the claimed invention. The instant application is therefore not entitled to an effective filing date earlier than **9.17.99**.

Applicant argues that the deposited microorganism(s) containing sequences can provide Applicant's claims with the necessary support, irrespective of the sequence information provided in the specification. As such the present claims should be deemed to enjoy the full priority date of December 23, 1998.

Applicant's are entitled to exactly the priority of what is disclosed in the prior application. As can be seen from the human sequence of PDE_XIV (SEQ ID NO : 2) as disclosed in United Kingdom 9828603.2, filed 12.23.98, had only **288 amino acids** as compared to instantly claimed human sequence of PDE_XIV (SEQ ID NO : 5) having 450 amino acids, Applicant did not have the full length sequence claimed as SEQ ID NO : 5. Therefore, the effective filing date for prior art purposes for SEQ ID NO : 5 is 9.17.99, and the following prior art rejection is maintained and repeated here.

Claim Rejections - 35 U.S.C. § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999(AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-2, 29-30 & 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Robison et al. (U.S.P. 6,146,876, filing date June 11, 1999). Robison et al. teach a human cyclic nucleotide sequence phosphodiesterase amino acid sequence of (SEQ ID NO : 1) which is 93.8% similar to the claimed amino acid sequence of SEQ ID NO : 5, and therefore having 75% or 85% homology (claims 29-30), or an amino acid sequence that comprises Z17 or SEQ ID NO : 21 (for example) [see sequence alignment of SEQ ID NO : 5 with SEQ ID NO : 1 from U.S.P. 6,146,876, enclosed here], the limitations of claim 1 & 2. Similarly, several amino acids or peptide sequences of Formula I are also comprised by the SEQ ID NO : 1 from U.S.P. 6,146,876. U.S.P. 6,146,876 also teaches a nucleic acid sequence of SEQ ID NO : 2, which is 94.1% similar to Applicants' SEQ ID NO : 6 [which encodes Applicants' human PDE of SEQ ID NO : 5], will therefore hybridize under high stringency conditions to a nucleic acid encoding a PDE protein of

claim 36. The reference anticipates the claims, since all the claim(s) limitations are taught in U.S.P. 6,146,876.

11. Claims drawn to SEQ ID NO : 5 (the elected invention) and the corresponding deposit will be in a better condition for allowance.

12. No claim is allowed.

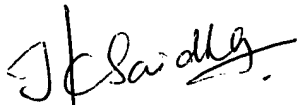
13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Tekchand Saidha
Primary Examiner, Art Unit 1652
August 26, 2003